Attorney Docket No. 1907.03 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors: Wettstein *et al.*	)	
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Application No.: 09/972,035	)	
	)	Group Art Unit: 1648
Filed: October 4, 2001	)	
	)	Examiner: M. Hill
For: Tsg101-GAGp6 INTERACTION AND USE THEREOF	)	
	)	
	)	

RESPONSE TO NOTIFICATION OF NON-COMPLIANT APPEAL BRIEF (37 C.F.R. § 41.37)

Mail Stop Appeal Brief - Patents
Commissioner for Patents
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Sir:

In accordance with MPEP § 1205.03(B), the following corrections are filed in response to the Notification of Non-Compliant Appeal Brief mailed August 11, 2006, the one-month period for response to which expires on September 11, 2006.

In the Notification, the instant Brief is deemed defective for allegedly failing to comply with 37 C.F.R. § 41.37(c)(1)(v). Specifically, the Notification alleges that the Brief is deficient in that "[c]laimed subject matter must seperately [sic] mapp [sic] each independent claim on appeal to [the] specification by page and line number or paragraph number."

The following Summary of Claimed Subject Matter corrects the Summary contained in the Brief as originally filed and brings the Brief into compliance with 37 C.F.R. § 41.37(c)(1)(v).

SUMMARY OF CLAIMED SUBJECT MATTER

The claimed invention relates to the inventors' discovery that the human tumor suppressor gene protein, Tsg101, interacts with the p6 portion of the human immunodeficiency virus type 1 (HIV1) GAG polyprotein (GAGp6), thereby forming an intermolecular protein-protein complex between Tsg101 and HIV GAG. See, e.g., Specification p. 6, ll. 22-27 & p. 14, Table 1. The interaction of these two proteins is required for the budding of HIV viral particles from host cells. Disruption of the interaction leads to the prevention of HIV budding and inhibition of HIV infection. Thus, the intermolecular protein-protein complexes can be used to screen for and identify compounds (drug candidates) that disrupt the interaction and are useful for treating HIV infection and AIDS. Importantly, the inventors further determined that the ubiquitin E2 variant (UEV) domain of the Tsg101 protein and the PTAP motif of the HIV GAGp6 late domain are responsible for the interactions See, e.g., Specification p. 38, ll. 5-6.

The rejected claims are drawn to (1) isolated protein complexes comprising Tsg101, fragments of Tsg101 comprising the UEV domain, or homologues thereof, interacting with HIV GAG, fragments of HIV GAG (such as GAGp6) comprising the late domain, or homologues thereof, (2) expression vectors encoding such interacting polypeptides, and (3) host cells containing such expression vectors. Importantly, the claims require that the claimed fragments of Tsg101 or HIV GAG must retain the ability to interact with a partner protein. The relevant claims also require that the homologous proteins have a certain percent amino acid sequence identity to Tsg101 or HIV GAG and retain the ability to interact with a partner protein.

Independent claim 1 is representative of those claims directed towards isolated protein complexes comprising a first protein interacting with a second protein (see, e.g., Specification p. 6, ll. 22-27 & p. 14, Table 1), wherein the first protein encompasses (a) full-length Tsg101 (see id. p. 81-83, Example 3), (b) a fragment thereof that comprises a UEV domain and interacts with an HIV GAGp6 late domain (see id. p. 14, Table 1 [reporting interaction between residues 7-390 of Tsg101 and HIV GAGp6], p. 9, ll. 25-28 [defining "protein fragment"], and p. 38, ll. 5-6 [indicating that "UEV domain of the Tsg101 protein and the PTAP motif of the HIV GAGp6 are responsible for the interactions"]), (c) a first polypeptide that interacts with an HIV GAGp6 late domain and

has an amino acid sequence that is at least about 75% identical to (a) or (b) (see id. at p. 11, l. 30 – p. 12, l. 8 [defining "homologue" to include full length proteins or fragments that are 75% identical to a native protein] & pp. 81-83, Example 3 [discussing experiments where homologous peptides created by mutagenesis of a native protein were found to interact]), and (d) a fusion protein comprising (a), (b), or (c) (see id. at p. 11, 21-29 [defining "fusion protein"], p. 79, l. 7 – p. 80, l. 8 [describing creation of fusion proteins for yeast two-hybrid assays] & p. 80, ll. 9-12 [noting that Tsg101 was one of the prey fusions found to interact]); and the second protein encompasses (i) full-length HIV GAG, (ii) a fragment thereof that comprises an HIV GAGp6 late domain and interacts with Tsg101 (see id. at p. 14, Table 1 [indicating a fragment of HIV GAG comprising amino acid residues 449-500 interacts with Tsg101], pp. 83-84, Example 4 [in which amino acid residues 1-207 of Tsg101 were found to interact with HIV GAGp6, and the interaction was disrupted by oligopeptides comprising amino acid residues 1-14 of the GAGp6 protein] & p. 9, ll. 25-28 [defining "protein fragment"]), (iii) a second polypeptide that interacts with Tsg101 and has an amino acid sequence that is at least about 75% identical to that of (i) or (ii) (see id. at p. 81, l. 27 – p. 82, l. 33 [including Tables 3 and 4, showing oligopeptides homologous to amino acid residues 1-14 of the GAGp6 protein that were used to competitively disrupt a protein complex between full-length GAGp6 and amino acid residues 1-207 of Tsg101]), and (iv) a fusion protein comprising (i), (ii), or (iii) (see id. at p. 11, ll. 21-29 [defining "fusion protein"] & p. 79, ll. 7-15 [describing creation of HIV GAGp6-Gal4 fusion protein]).

Independent Claim 44 is representative of the claims drawn towards expression vectors and comprises two distinct expression vectors designed to express a first protein and a second protein, respectively. See Specification, p. 43, l. 24 – p. 45, l. 9 & generally, p. 62, l. 14 – p. 70, l. 13. In claim 44, the first nucleotide expression vector has a nucleic acid encoding a first protein (see, e.g., id. at p. 79, l. 16 – p. 80, l. 12 [describing creation of expression vectors from prey library, including one that contained Tsg101]), which is selected from the group consisting of (i) full-length Tsg101, (ii) a fragment thereof that comprises a UEV domain and interacts with an HIV GAGp6 late domain, (iii) a first polypeptide having an amino acid sequence at least about 75% identical to that of (i) or (ii), and that interacts with an HIV GAGp6 late domain, and (iv) a first fusion

protein comprising (i), (ii), or (iii). In claim 44, the second nucleotide expression vector has a nucleic acid encoding a second protein (see, e.g., id. at p. 79, ll. 7-15 [describing creation of HIV GAGp6-Gal4 expression vector]), which is selected from the group consisting of (1) full-length HIV GAG, (2) full-length HIV GAGp6, (3) a fragment of (1) or (2) that interacts with Tsg101, (4) an HIV GAGp6 fragment that comprises an HIV GAGp6 late domain motif and interacts with Tsg101, (5) a second polypeptide that has an amino acid sequence at least about 75% identical to that of (1), (2), (3), or (4), and that interacts with Tsg101, and (6) a second fusion protein comprising (1), (2), (3), (4), or (5). Furthermore, Claim 44 requires that the first and second proteins must interact to form a protein complex.

Independent Claim 45 is representative of those claims directed to host cells comprising a composition substantially equivalent to the one recited in Claim 44. See, e.g., Specification, p. 81, l. 14 – p. 82, l. 19 (describing co-transformation of a host cell with two vectors encompassed by Claim 44).

Independent Claim 61 reads upon an expression vector comprising a first and second nucleic acid, wherein said first and second nucleic acids encode a first and second protein, respectively, wherein said encoded proteins are substantially identical to those recited in Claim 44, and wherein said first and second proteins interact to form a protein complex. See, e.g., Specification, p. 62, l. 14 – p. 63, l. 15, p. 79, l. 16 – p. 80, l. 12 (describing creation of expression vectors from prey library, including one that contained Tsg101), p. 79, ll. 7-15 (describing creation of HIV GAGp6-Gal4 expression vector) & p. 67, ll. 14-17 (artisans would recognize that the two nucleic acids could easily be combined into, and expressed from, a single vector).

Independent Claim 63 is drawn to a non-human host cell expressing a first and a second protein substantially identical to those of Claim 1, wherein said first and second proteins must interact to form a protein complex within said non-human host cell. See, e.g., Specification, p. 81, l. 14 – p. 82, l. 19 (describing co-transformation of a non-human, yeast host cell with two vectors encompassed by Claim 44).

Independent Claim 64 is substantially identical to Claim 63 except that, in this case, the host cell must be an isolated human host cell. See, e.g., Specification, p. 45, ll.

6-9 (vectors may be expressed in a variety of cells, including human cells) & p. 80, ll. 14-22 (proteins are expressed in a human host cell).

Note that the passages cited above are exemplary and do not represent a comprehensive listing of where support for a particular claim, element or aspect can be found. Further support for the subject matter of the independent claims can be found throughout the specification. In addition, the table below shows where passages of support can be found for specific elements and aspects of the claims. Further note that the passages cited in this table are also exemplary, and do not represent a comprehensive listing of where support for a particular element or aspect can be found.

Table 1. Location of support for claim elements within the as-filed specification

Element Or Aspect	Description / Identity / Characteristics	Location of Support in the Specification
1	Protein complexes comprising human Tsg101 interacting with HIV1 GAGp6	Table 1, p. 14; Example 1, pp. 79-80; and Example 3, pp. 81-83
2	Entrez nucleotide accession numbers encoding amino acid sequences of human Tsg101 and HIV1 GAGp6	Table 1, p. 14
3	Fragments of interacting proteins that retain the ability to interact	p. 38, ll. 5-6 & 27-29; p. 39, ll. 2-4 & 23-25; p. 40, ll. 23-27; and Example 4, pp. 83-84
4	Homologous proteins that retain the ability to interact	p. 11, l. 30 – p. 12, l. 13; and Example 3, pp. 81-83
5	Percent identity of homologous proteins	p. 12, l. 14 – p. 13, l. 4
6	Fusion proteins (general)	p. 11, ll. 21-29
7	Interactions & interaction domain (general)	p. 10, ll. 14-28
8	Protein complex & isolated protein complexes (general)	p. 10, l. 29 – p. 11, l. 20
9	Determining whether proteins interact	p. 10, ll. 14-23; and p. 61, l. 23 – p. 75, l. 17
10	In vitro screening/binding assays	p. 58 l. 18 – p. 61, l. 14; Example 4, pp. 83-84; and Figures 2, 3, and 4
11	In vivo screening/binding assays; esp. yeast two-hybrid assays	p. 61, l. 16 – p. 75, l. 17; Example 1, pp. 79-80, l. 12; and Example 3, pp. 81–83
12	Expression vectors	Section 4.3.1.1., p. 62-69

Element Or Aspect	Description / Identity / Characteristics	Location of Support in the Specification
13	Reporters	Section 4.3.1.2., p. 70-72
14	Fusion proteins having DNA binding domains	p. 70, ll. 19-24; Example 1, pp. 79-80, l. 12; and Example 3, pp. 81–83
15	Fusion proteins having transcription-activating domains	p. 70, ll. 19-24; Example 1, pp. 79-80, l. 12; and Example 3, pp. 81–83
16	Host cells for detecting protein-protein interactions	p. 45, ll. 6-9; p. 63, ll. 16-21; p. 64, ll. 14-19; p. 66, l. 27 – p. 67, l. 13; p. 69, l. 21 – p. 70, l. 13; Example 1, pp. 79-80, l. 12; and Example 3, pp. 81–83
17	The UEV domain of Tsg101	p. 33, ll. 26-27; p. 35, ll. 1-2 & 18-26; and p. 38, ll. 5-6 & 26-29
18	The late domain of HIV GAGp6 and viral budding	p. 33, l. 30 – p. 34, l. 10; p. 34, ll. 29-31; p. 36, l. 16 – p. 37, l. 16
19	The P(T/S)AP and P(T/S/I)(A/T)P motifs of viral GAG proteins	p. 34, ll. 11-31; p. 35, l. 18 – p. 37, l. 16; p. 39, l. 1 – p. 40, l. 27; and Example 3, pp. 81-83

CONCLUSION

It is believed that, upon entry of the new "Summary of Claimed Subject Matter" presented above, the corrected Brief will be in compliance with the requirements of 37 C.F.R. § 41.37(c)(1)(v). Should the Examiner determine that additional issues remain which might be resolved by a telephone conference, he is respectfully invited to contact the undersigned representative of the Applicants.

It is also believed that neither an extension of time or fee is required for filing this response. If this is incorrect, an extension of time as deemed necessary is hereby requested, and the Commissioner is hereby authorized to charge any appropriate fees or deficiency, or to credit any over payment to Deposit Account no. **50-1627**.

Respectfully submitted,

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